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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,852	12/10/2003	Frederick L. Hall	14230-010002	4628

20985 7590 05/08/2007
FISH & RICHARDSON, PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
DEBERRY, REGINA M	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
05/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/733,852	HALL ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *66-69 and 72-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-69 and 72-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

Applicant's arguments filed 20 February 2007 have been entered in full. Claims 1-65, 70, 71 are cancelled. Claims 66-69 and 72-80 are pending and under examination.

Withdrawn Objections And/Or Rejections

The rejection to claims 66-69 and 72-80 under 35 U.S.C. 112, first paragraph, enablement, as set forth at pages 5-9 of the previous Office Action (22 November 2006), is *withdrawn*.

Claim Rejections - 35 U.S.C. § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 66-69, 72-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the instant claims:

wherein an epithelial cell proliferation-modulating agent is insulin, nerve growth factor (NGF), NGF receptor, epidermal growth factor (EGF) receptor, neu, inhibin a, inhibin b, wnt-2 and hepatocyte growth factor (HGF) receptor (c-met),

does not reasonably provide enablement for the instant claims:

wherein an epithelial cell proliferation-modulation agent is Mullerian inhibitory substance, tumor necrosis factor (TNF) receptor (type 1) and tumor necrosis factor (TNF) receptor (type 2).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification states that the present invention provides new compositions and methods to induce repair of epithelial tissue by specifically targeting tissue in need of such repair with a fusion polypeptide of the invention. The invention promotes localized wound healing by providing a cell proliferation-modulation agent fused to a collagen-binding domain (page 3, lines 15-23). The specification states that the present invention provides a recombinant fusion polypeptide comprising EGF and an appropriate collagen-binding domain for enhancing the effective local concentration of EGF at the site of tissue injury thereby promoting repair of damaged intestinal mucosa in animal models and, ultimately in humans (page 8, lines 16-24). The specification states that an epithelial cell proliferation-modulating agent is any agent that can promote or inhibit epithelial growth or differentiation (page 10, lines 14-20). The specification teaches epidermal growth factor (EGF) as a protein with epithelial cell proliferation activity. The examples teach the construction of a fusion protein comprising a collagen binding domain and EGF. The examples demonstrate that the fusion protein promotes epithelial cell growth in wound healing.

The instant examples and the art of record fail to teach that a fusion protein comprising a collagen-binding domain and Mullerian inhibitory substance, TNF receptor (type 1) or TNF receptor (type 2) can promote or inhibit epithelial growth or differentiation. Claim 80 is drawn to a pharmaceutical composition comprising the claimed fusion proteins and thus reads on *in vivo* treatment. The instant examples demonstrate the efficacy of a fusion protein comprising a collagen binding domain and EGF in an animal model for experimental colitis (Figures 6 and 7). The specification fails to disclose a correlation (any working examples, animal models, etc.) between the use of the instant invention and a treatment in subjects. It could not be predicted that the data presented in the specification would be in any way correlative with therapeutic agents comprising the instant fusion protein for *in vivo* treatments.

Applicant states that the present Office Action is unclear as to what is enabled or not enabled. Applicant submits that the Office Action mailed June 22, 2006, stated that the claims were enabled for nerve growth factor. Applicant argues that the enablement rejection is met if the description enables any mode of making and using the invention. Applicant cites case law and *In re Wands*. Applicant discusses the claims and the instant specification. Applicant argues that the Examiner has provided no evidence as to why one of skill in the art would be unable to make and use the invention. Applicant discusses the references of record, specifically Kurada et al., Kollias et al. and Dale et al.

Applicant's arguments have been fully considered but are not deemed persuasive. The question is not whether one of skill in the art can make the instant

invention. The question is whether one of skill in the art can use the instant invention for the claimed activity (i.e. epithelial cell proliferation-modulating activity).

Contrary to Applicant's assertion, the Examiner provided evidence as to why one of skill in the art would be unable to use the instant invention. The specification only demonstrates epidermal growth factor (EGF), **an unclaimed species**, as a protein with epithelial cell proliferation activity. The specification need not contain examples of the invention if disclosed in a manner where one skilled in the art could practice without undue experimentation, but it is considered a factor involving unpredictability. The instant examples fail to teach that Mullerian inhibitory substance and TNF receptors (type 1 and type 2) have the biological activity of epithelial cell proliferation-modulation. The specification fails to teach how to use the instant invention, which lacks the claimed biological functions.

The Examiner stated why the art of record contributes to the unpredictability of the instant invention. Kollias et al. teach that two TNF receptors are known to mediate either in cooperation or independently, a wide spectrum of cellular responses ranging from proliferation and differentiation to cytotoxicity or apoptosis. Kollias et al. fail to teach epithelial cell proliferation-modulation activity (promotion/inhibition of epithelial growth or differentiation) for TNF receptors type 1 and/or 2. Behringer (reference submitted by Applicant) teaches that Mullerian inhibiting substance inhibits the the development of mullerian ducts. Behringer fails to teach epithelial cell proliferation-modulation activity (promotion/inhibition of epithelial growth or differentiation). There is no evidence to believe that the instant invention would have the claimed activity. The

scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
4/27/07

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER

AU1647 5/3/07